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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,534	08/31/2005	Peter Serno	Le A 35 683	8954

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Barbara A. Shimci
Director, Patents & Licensing
Bayer HealthCare LLC - Pharmaceuticals
555 White Plains Road, Third Floor
Tarrytown, NY 10591

EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,534	SERNO ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *6,8-10 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7 and 11-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/14/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response to Restriction/Election requirement and Applicant's Arguments/Remarks filed 05/01/09 is acknowledged. Receipt of the Preliminary Amendment and the Information Disclosure Statement (IDS), both filed 01/14/05 is also acknowledged.

Applicant's election with traverse of Group II (claims 1-5, 7 & 11-15) in the reply filed on 01 May 2009 is acknowledged. The traversal is on the ground(s) that "a coated tablet is a form of the medicaments obtainable by the methods of this invention and that a search for the method and medicament of Group II would necessarily yield the methods and medicaments recited in Group I and would unavoidably be coextensive". This is not found persuasive because the different groups would require completely different searches in both patent- and non-patent databases and there is no expectation that the searches would be coextensive in scope. The different groups also represent unique classes and subclasses (Group I 424/400; Group II 424/474) and are capable of supporting a separate patent within the art based on their different classification. Moreover, the medicament of Group I does not have to be in the form of a "coated tablet" as is claimed in Group II. Group I can be in various forms, such as in the form of a capsule or pellet or lozenge, for example. Group I can also be administered via routes other than the oral route, i.e., for nasal or topical application. The requirement is still deemed proper and is therefore made FINAL.

Applicant's election with traverse of species (a) sexual dysfunctions in the reply filed on 01 May 2009 is also acknowledged. The traversal is on the ground(s) that "it is known in the art that erectile dysfunction is a form of sexual dysfunctions". This argument was found persuasive.

Accordingly, the election of species requirement between erectile dysfunction and sexual dysfunctions has been withdrawn. However, the restriction requirement between Groups I and II has been maintained, as noted above.

Claims 6, 8-10 and 16 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 01 May 2009.

Claims 1-16 are pending in this action. Claims 1, 3 and 5-10 have been amended. New claims 11-16 have been added. Claims 1-5, 7 and 11-15 have been examined in this action. Claims 6, 8-10 and 16 have been withdrawn. Claims 1-5, 7 and 11-15 are rejected.

* * * * *

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 14 January 2005 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

* * * * *

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7 and 11-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation

(1) The nature of the invention/(5) The breadth of the claims:

The instant invention is directed to a method for producing medicaments comprising vardenafil hydrochloride trihydrate in solid form; a coated tablet obtainable by the method and a method for the treatment and/or prophylaxis sexual dysfunctions and erectile dysfunction.

(2) The state of the prior art:

The prior art teachings provide for the treatment of sexual dysfunctions comprising a preparation that includes an active ingredient, such as a PDE inhibitor, preferably a cGMP PDE inhibitor, used for the treatment of sexual dysfunctions. See for instance, WO Abstract 01/19357 (Bischoff et al.).

(3) The relative skill of those in the art:

The relative skill of those in the art is very high, i.e., MD or Ph.D.-level technology.

(4) The predictability or unpredictability of the art:

The unpredictability of the art is high. Prior art formulations recognize compositions for the treatment of sexual dysfunctions based on the inclusion of a cGMP PDE inhibitor, but do not recognize nor teach that the compositions provide for the 'prophylaxis' or 'prevention' of such sexual dysfunctions. (See WO 01/19357 Abstract - Bischoff et al.).

(6) The amount of direction or guidance presented:

The specification filed 01/14/05, discloses the "treatment and/or prophylaxis" of sexual and erectile dysfunctions based on a medicament comprising vardenafil hydrochloride trihydrate. While it is clear to the Examiner as to how the active ingredient (vardenafil hydrochloride trihydrate) can be used for the effective "treatment" of sexual dysfunctions, it is unclear as to how the "prophylaxis" of such sexual dysfunctions would occur. Particularly, since the prior art recognizes and teaches the same active ingredient (vardenafil hydrochloride) for the treatment of sexual dysfunctions is permissible based on administration of the active ingredient, but does not teach the prophylaxis of sexual dysfunctions given the same active agent. The specification provides no guidance on how the prevention of sexual dysfunctions can be provided through the use of the claimed active ingredient - vardenafil hydrochloride trihydrate. The prior art demonstrates treatment (of sexual dysfunctions) is possible but not the prevention thereof.

(7) The presence or absence of working examples:

The working examples are insufficient to establish the instant method for the prophylaxis of sexual dysfunctions and erectile dysfunction. The examples focus on the preparation and production of medicaments comprising vardenafil hydrochloride trihydrate in solid form but do not discuss in detail as to how the prophylaxis of sexual dysfunctions would be obtained given the instant medicament and method. In addition, the examples are distinct from the scope of the claims and there are no formulations of the claims presented. For instance, the examples demonstrate that the use of coating agents (i.e., hypromellose, macrogol) and disintegrants (i.e., crospovidone) are needed but the instant claims are not representative of the examples of the specification. Therefore, the working examples are insufficient to establish the instant method for the prophylaxis of sexual dysfunctions and erectile dysfunction.

(8) The quantity of experimentation necessary:

When the above factors are weighed together, it is the position of the Examiner that the instant invention would require 'undue' and painstaking experimentation to arrive at the instant invention in order to determine which particular ingredients and combinations of elements would be required in order to effectively treat sexual dysfunctions (i.e., erectile dysfunction), with the "prevention" or "prophylaxis" of sexual dysfunctions being less probable.

Note: Deletion of the term "and/or prophylaxis" as currently recited in claims 14 and 15, would be sufficient to overcome this rejection.

* * * * *

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7 and 11-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants claim a method for producing medicaments comprising vardenafil hydrochloride trihydrate in solid form; a coated tablet obtainable by the method and a method for the treatment and/or prophylaxis of sexual dysfunctions and erectile dysfunction. The process steps and written description are insufficient and have not been presented in such a way as to allow one of ordinary skill in the art to understand and practice the invention. For instance, the method of production of claim 1 and the scope of the claims is distinct from the examples presented in the specification. For instance, the examples demonstrate that the use of coating agents (i.e., hypromellose, macrogol) and disintegrants (i.e., microcrystalline cellulose, crospovidone) are needed as a critical part of the manufacturing process but the instant claims are not representative of the examples provided in the specification. No specific formulations and specific procedures have been set forth to allow one of ordinary skill to know how to carry out a method for producing medicaments comprising vardenafil hydrochloride trihydrate in solid form and a coated tablet which would yield from the stated method of production.

* * * * *

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5, 7 and 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niewöhner *et al.* (hereinafter "Niewöhner") (U.S. Pat. No. 6,362,178).

Niewöhner ('178) teaches 2-phenyl substituted imidazotriazinones as phosphodiesterase inhibitors, methods for their preparation, compounds obtained therefrom and their use as pharmaceuticals. The compounds inhibit cGMP-metabolizing phosphodiesterases and are suitable for use as active compounds in pharmaceuticals, for the treatment of disorders, such as disorders of the urogenital system, in particular for the treatment of erectile dysfunction (see Abstract); (col. 1, lines 5-55); (col. 30, line 49 – col. 31, line 4). The compounds, in particular the salts, may also be present as hydrates. Such compounds may typically contain 1 to 5 equivalents of water. Hydrates can be prepared, for example, by crystallizing the compound from water or a water-containing solvent (col. 9, lines 18-24). Reaction temperatures for

preparation of the compounds is disclosed at column 28, lines 44-67). Niewöhner teaches that the active compounds and their physiologically acceptable salts (for example hydrochlorides) can be converted in a known manner into the customary formulations, such as tablets, coated tablets, pills, granules and the like (col. 32, lines 6-25). The Examples demonstrate various preparation methods for the 2-phenyl substituted imidazotriazinones.

The instant invention when taken as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, given the teachings of Niewöhner. Niewöhner discloses 2-phenyl substituted imidazotriazinones as phosphodiesterase inhibitors, methods for their preparation and their use as pharmaceuticals. The compounds can be present as hydrates and can contain 1 to 5 equivalents of water. Hydrates can be prepared, for example, by crystallizing the compound from water or a water-containing solvent. The compounds are particularly useful for the treatment of sexual dysfunctions, such as erectile dysfunction. Niewöhner further teaches that the active compounds can be provided in the form of coated tablets and can be administered via various routes (i.e., oral administration).

* * * * *

Claims 1-5, 7 and 11-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niewöhner *et al.* alone (hereinafter "Niewöhner") (U.S. Pat. No. 6,362,178) or in view of Bischoff *et al.* (hereafter "Bischoff") (WO 01/19357).

The teachings of Niewöhner are discussed above.

Bischoff is further relied upon for their teaching of a combination preparation for the treatment of sexual dysfunctions comprising at least one active ingredient being a PDE inhibitor, preferably a cGMP PDE inhibitor, in combination with a lipid-reducing agent, whereby the

preparation is useful for the treatment of sexual dysfunctions. The active ingredients can be provided as a functional unit or separated from each other (see Abstract). While claim 14, drawn to the "treatment of erectile dysfunction" is not disclosed in the Abstract of Bischoff, Bischoff nonetheless teaches treatment of the generic 'sexual dysfunctions' and thus, this would be all-inclusive of the species-specific "erectile dysfunction" claimed by Applicant, as it is known in the art that erectile dysfunction is a form of sexual dysfunction (as evidenced in Applicant's specification, page 8, lines 8-12). Hence, "erectile dysfunction" would be encompassed in the generic grouping of sexual dysfunctions taught by Bischoff. Thus, the limitations of claims 14 and 15 are met by the teachings of Bischoff, who explicitly teaches treatment of sexual dysfunctions based on administration of a cGMP PDE inhibitor.

It would have been obvious to one of ordinary skill in the art to employ a cGMP PDE inhibitor, as taught by Bischoff, within the preparations of Niewöhner. One would do so with a reasonable expectation of success as Bischoff teaches a composition comprising a cGMP PDE inhibitor which is known to be effective for the treatment of sexual dysfunctions. The expected result would be an improved method for treating sexual dysfunctions (i.e., erectile dysfunction) in a subject in need thereof.

* * * * *

Conclusion

--No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday-Friday during regular business hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Humera N. Sheikh/

Primary Examiner, Art Unit 1615

hns

August 3, 2009